

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

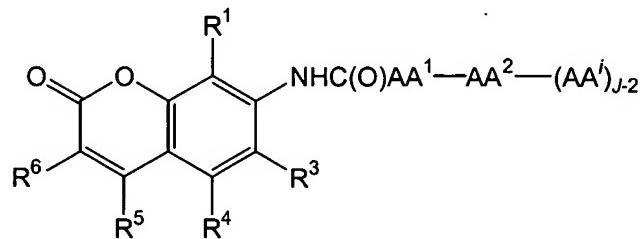
Listing of Claims:

1 **1** (cancelled)

1 **2** (currently amended) The material according to claim 5, wherein said linking
2 group R¹⁴ is a member selected from the group consisting of substituted or unsubstituted alkyl,
3 substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl.

1 **3-4** (cancelled)

1 **5** (currently amended): A material having the structure:



2 wherein:

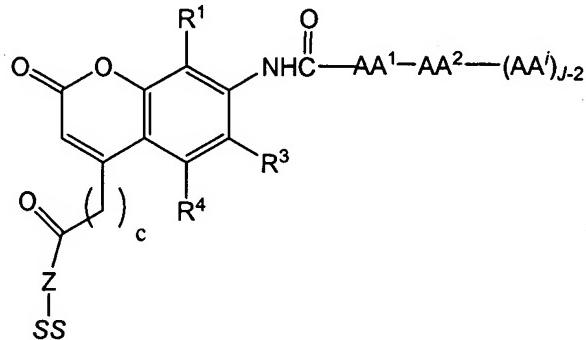
4 R¹, R³, R⁴, R⁵ and R⁶ are members independently selected from the group
5 consisting of H, halogen, -NO₂, -CN, -C(O)_mR⁷, -C(O)NR⁸R⁹, -S(O)_nR¹⁰,
6 -SO₂NR¹¹R¹², -OR¹³, substituted or unsubstituted alkyl and -R¹⁴-SS, with
7 the proviso that at least one of R¹, R³, R⁴, R⁵ and R⁶ is -R¹⁴-SS;

8 wherein:

9 R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ are members independently selected from
10 the group consisting of H, substituted or unsubstituted alkyl and
11 substituted or unsubstituted aryl;

12 R¹⁴ is a linking group adjoining said fluorogenic moiety and said solid
13 support;
14 m is a member selected from the group consisting of the integers 1 and 2;
15 t is a member selected from the group consisting of the integers from 0 to
16 2; and
17 SS is a solid support;
18 AA¹-AA²-(AAⁱ)_{J-2} is a peptide sequence, wherein each of AA¹ through AAⁱ is an
19 amino acid residue which is a member independently selected from the
20 group of natural amino acid residues, unnatural amino acid residues and
21 modified amino acid residues;
22 J denotes the number of amino acid residues forming said peptide
23 sequence and is a member selected from the group consisting of
24 the numbers from 2 to 10, such that J-2 is the number of amino
25 acid residues in the peptide sequence exclusive of AA¹-AA²; and
26 i denotes the position of said amino acid residue relevant to AA¹ and when
27 J is greater than 2, i is a member selected from the group
28 consisting of the numbers from 3 to 10.

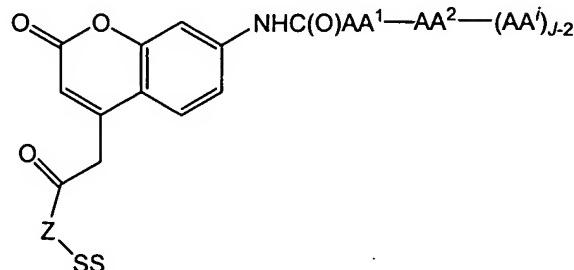
1 6 (currently amended): The material according to claim 5, having the structure:



2 wherein: Z is a member selected from the group consisting of -O-, and --NR¹⁶-,
3 wherein R¹⁶ is H, substituted or unsubstituted alkyl and substituted or
4 unsubstituted aryl, and
5

6 c is a member selected from the integers from 0 to 6.

1 **7** (currently amended): A material according to claim 6, having the structure:



1 **8** (currently amended): A method of assaying for the presence of an
2 enzymatically active protease in a sample, said method comprising:

3 (a) contacting said sample with a material according to claim 5 in such a manner
4 whereby said fluorogenic moiety is released from said peptide sequence upon action of said
5 protease, thereby producing a fluorescent moiety; and

6 (b) observing whether said sample undergoes a detectable change in fluorescence,
7 said detectable change being an indication of the presence of said enzymatically active protease
8 in said sample.

1 **9** (original): The method according to claim 8, wherein said protease is a
2 member selected from the group consisting of aspartic protease, cysteine protease,
3 metalloprotease and serine protease.

1 **10** (original): The method according to claim 8, wherein said protease is a
2 protease of a microorganism.

1 **11** (original): The method according to claim 10, wherein said microorganism is
2 a member selected from the group consisting of bacteria, fungi, yeast, viruses, and protozoa.

1 **12** (original): The method according to claim 8, wherein said sample is a clinical
2 sample from a subject.

1 **13** (original): The method according to claim 8, further comprising (c)
2 quantifying said fluorescent moiety, thereby quantifying said protease.

1 **14** (currently amended): A method of assaying for the presence of a selected
2 microorganism in a sample by probing the sequence specificity of peptide cleavage by a protease
3 of said microorganism, said method comprising:

4 (a) contacting a sample suspected of containing said selected microorganism with
5 a material according to claim 5, wherein said peptide comprises a
6 sequence that is selectively cleaved by said protease of said selected
7 microorganism, thereby releasing the fluorogenic moiety from the peptide
8 sequence;

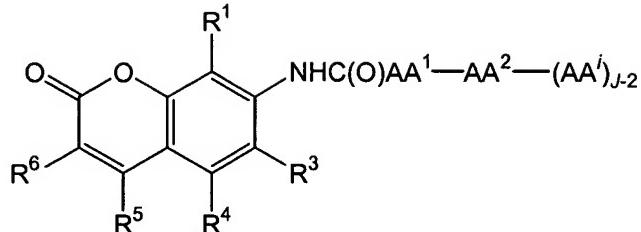
9 (b) detecting the cleavage by detecting fluorescence arising from a fluorescent
10 moiety produced by cleavage of said fluorogenic moiety from said peptide
11 sequence, thereby confirming said presence of said selected
12 microorganism in said sample.

1 **15** (original): The method according to claim 14, further comprising (c)
2 quantifying said fluorescence, thereby quantifying said protease of said microorganism.

16 (cancelled)

1 **17** (currently amended): The fluorogenic peptide according to claim 18, wherein
2 Y is an organic functional group selected from the group consisting of -COOR¹⁷, CONR¹⁷R²¹,
3 -C(O)R¹⁷R²¹, -OR¹⁷, -SR¹⁷, -C(O)SR¹⁷ and -NR¹⁷R²¹
4 wherein, R¹⁷ and R²¹ are members independently selected from H, substituted or
5 unsubstituted alkyl and substituted or unsubstituted aryl.

1 **18** (currently amended): A fluorogenic peptide having the structure:



3 wherein:

4 R^1, R^3, R^4, R^5 and R^6 are members independently selected from the group
5 consisting of H, halogen, $-NO_2$, $-CN$, $-C(O)_mR^{6'}$, $-C(O)NR^7R^8$, $-S(O)_tR^9$,
6 $-SO_2NR^{10}R^{11}$, $-OR^{12}$, substituted or unsubstituted alkyl, $-NHC(O)-P$, and –
7 $R^{20}-Y$, with the proviso that at least one of R^1, R^3, R^4, R^5 and R^6 is $-R^{20}-Y$,

8 wherein:

9 $R^{6'}, R^7, R^8, R^9, R^{10}, R^{11}$ and R^{12} are members independently selected from
10 the group consisting of H, substituted or unsubstituted alkyl and
11 substituted or unsubstituted aryl;

12 R^{20} is either present or absent and is a member selected from the group
13 consisting of substituted or unsubstituted alkyl and substituted or
14 unsubstituted heteroalkyl;

15 Y is a member selected from the group consisting of organic functional
16 groups and methyl;

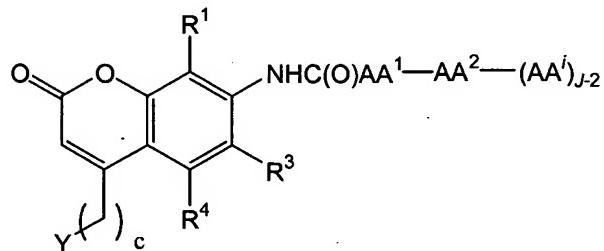
17 m is a member selected from the group consisting of the integers 1 and 2;
18 and

19 t is a member selected from the group consisting of the integers from 0 to
20 2.

21 $AA^1-AA^2-(AA^i)_{J-2}$ is a peptide sequence, wherein each of AA^1 through AA^i is an
22 amino acid residue which is a member independently selected from the
23 group of natural amino acid residues, unnatural amino acid residues and
24 modified amino acid residues;

25 *J* denotes the number of amino acid residues forming said peptide
26 sequence and is a member selected from the group consisting of
27 the numbers from 2 to 10, such that *J*-2 is the number of amino
28 acid residues in the peptide sequence exclusive of AA¹-AA²; and
29 *i* denotes the position of said amino acid residue in sequence relative to
30 AA¹ and when *J* is greater than 2, *i* is a member selected from the
31 group consisting of the numbers from 3 to 10.

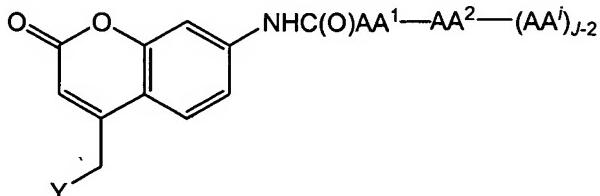
1 **19** (original): A fluorogenic peptide according to claim **18**, having the structure:



2 wherein:

3 *c* is a member selected from the group consisting of the integers from 0 to 6.

1 **20** (original): A fluorogenic peptide according to claim **19**, having the structure:



1 **21** (original): The fluorogenic peptide according to claim **18**, wherein said
2 peptide sequence comprises a peptide bond that is cleaved by a protease releasing said
3 fluorogenic moiety from said peptide sequence, thereby producing a fluorescent moiety and a
4 peptide moiety.

1 **22** (original): The fluorogenic peptide according to claim **21**, wherein said
2 peptide bond is formed between a carboxyl of the carboxy-terminus amino acid residue and an
3 amine group of said fluorogenic moiety.

1 **23** (currently amended): A method of assaying for the presence of an
2 enzymatically active protease in a sample, said method comprising:

3 (a) contacting a sample suspected of containing said protease with a peptide
4 according to claim **18** in such a manner whereby said fluorogenic moiety is released from said
5 peptide sequence upon action of said protease, thereby producing a fluorescent moiety; and
6 (b) observing whether said sample undergoes a detectable change in fluorescence,
7 said detectable change being an indication of the presence of said enzymatically active protease
8 in said sample.

1 **24** (original): The method according to claim **23**, wherein said protease is a
2 member selected from the group consisting of aspartic protease, cysteine protease,
3 metalloprotease and serine protease.

1 **25** (original): The method according to claim **23**, wherein said protease is a
2 protease of a microorganism.

1 **26** (original): The method according to claim **25**, wherein said microorganism is
2 a member selected from the group consisting of bacteria, fungi, yeast, viruses, and protozoa.

1 **27** (original): The method according to claim **23**, wherein said sample is a
2 clinical sample from a subject.

1 **28** (original): The method according to claim **27**, wherein said subject is a
2 human.

1 **29** (original): The method according to claim **23**, further comprising (c)
2 quantifying said fluorescent moiety, thereby quantifying said protease.

1 **30** (currently amended): A method of assaying for the presence of a selected
2 microorganism in a sample by probing the sequence specificity of peptide cleavage by a protease
3 of said microorganism, said method comprising:

4 (a) contacting a sample suspected of containing said selected microorganism with
5 a material according to claim **18**, wherein said peptide comprises a
6 sequence that is selectively cleaved by a protease of a selected
7 microorganism, thereby releasing said fluorogenic moiety from said
8 peptide sequence;

9 (b) detecting said cleavage by detecting fluorescence arising from a fluorescent
10 moiety produced by cleavage of said fluorogenic moiety from said peptide
11 sequence, thereby confirming said presence of said selected
12 microorganism in said sample.

1 **31** (original): The method according to claim **30**, further comprising (c)
2 quantifying said fluorescence, thereby quantifying said protease of said microorganism.

1 **32** (cancelled)

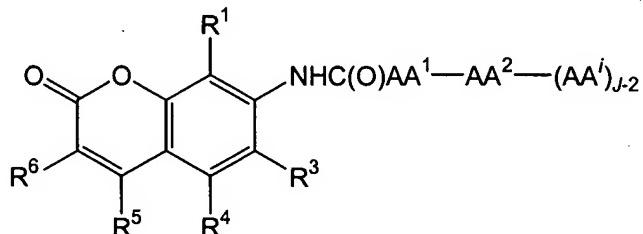
33 (currently amended): The library according to claim **35**, wherein said linking group R¹⁴ is a member selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl and substituted or unsubstituted aryl.

1 **34** (currently amended): The library according to claim **35**, wherein Y is an
2 organic functional group selected from the group consisting of -COOR¹⁷, CONR¹⁷R²¹,
3 -C(O)R¹⁷R²¹, -OR¹⁷, -SR¹⁷, -C(O)SR¹⁷, and -NR¹⁷R²¹
4 wherein, R¹⁷ and R²¹ are members independently selected from H, substituted or
5 unsubstituted alkyl and substituted or unsubstituted aryl.

Amdt. dated March 9, 2005

Reply to Office Action of September 9, 2004

1 **35** (currently amended): A library of fluorogenic peptides comprising at least a
2 first peptide having a first peptide sequence covalently attached to a first fluorogenic moiety and
3 a second peptide having a second peptide sequence covalently attached to a second fluorogenic
4 moiety, said first peptide and said second peptide having the structure:



6 wherein:

7 R¹, R³, R⁴, R⁵, and R⁶ are members independently selected from the group
8 consisting of H, halogen, -NO₂, -CN, -C(O)_mR⁷, -C(O)NR⁸R⁹, -S(O)_nR¹⁰,
9 -SO₂NR¹¹R¹², -OR¹³, substituted or unsubstituted alkyl, -NH-C(O)-P,
10 R²⁰-Y and -R¹⁴-SS, with the proviso that for each peptide at least one of
11 R¹, R³, R⁴, R⁵ and R⁶ is a member independently selected from -R¹⁴-SS
12 and R²⁰-Y,

13 wherein:

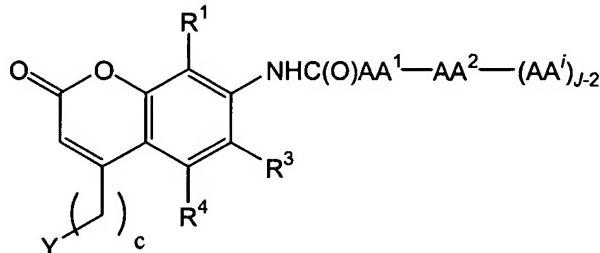
14 R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ are members independently selected from
15 the group consisting of H, substituted or unsubstituted alkyl and
16 substituted or unsubstituted aryl;
17 R¹⁴ is a linking group adjoining said fluorogenic moiety and the solid
18 support;

19 R²⁰ is either present or absent and is a member selected from the group
20 consisting of substituted or unsubstituted alkyl and substituted or
21 unsubstituted heteroalkyl;

22 Y is a member selected from the group consisting of organic functional
23 groups and methyl;

24 m is a member selected from the group consisting of the integers from 1 to
25 2;
26 t is a member selected from the group consisting of the integers from 0 to
27 2; and
28 SS is a solid support;
29 AA¹-AA²-(AAⁱ)_{J-2} is a peptide sequence, wherein each of AA¹ through AAⁱ is an
30 amino acid residue which is a member independently selected from the
31 group of natural amino acid residues, unnatural amino acid residues and
32 modified amino acid residues;
33 J denotes the number of amino acid residues forming said peptide
34 sequence and is a member selected from the group consisting of
35 the numbers from 2 to 10, such that J-2 is the number of amino
36 acid residues in the peptide sequence exclusive of AA¹-AA²; and
37 i denotes the position of said amino acid residue in sequence relative to
38 AA¹ and when J is greater than 2, i is a member selected from the
39 group consisting of the numbers from 3 to 10.

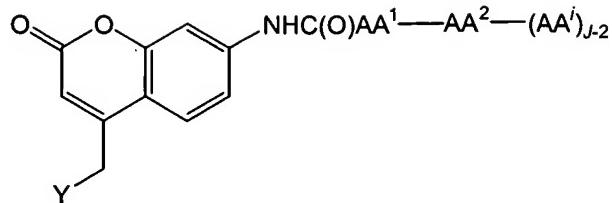
1 36 (currently amended): The library of fluorogenic peptides according to claim
2 35, wherein said first peptide and said second peptide have the structure:



4 wherein:

5 c is a member selected from the group consisting of the numbers from 0 to 6.

1 37 (original): The library of fluorogenic peptides according to claim 36, wherein
2 said first peptide and said second peptide have the structure:



1 **38** (currently amended): The library according to claim **35**, wherein said
2 fluorogenic moiety of said first peptide and said fluorogenic moiety of said second peptide are
3 different fluorogenic moieties.

1 **39** (currently amended): The library according to claim **35**, wherein said first
2 peptide sequence and said second peptide sequence are identical.

1 **40** (currently amended): The library according to claim **35**, wherein said first
2 peptide sequence and said second peptide sequence are different.

1 **41** (currently amended): The library according to claim **40**, wherein an amino
2 acid residue selected from the group consisting of AA¹, AA², AAⁱ and combinations thereof of
3 said first peptide is a different amino acid residue than an amino acid residue at a corresponding
4 position relative to AA¹ of said second peptide.

1 **42** (currently amended): The library according to claim **35**, wherein AA¹ of said
2 first peptide sequence and AA¹ of said second peptide sequence are identical amino acid
3 residues.

1 **43** (currently amended): The library according to claim **35**, wherein AA¹ of said
2 first peptide sequence and AA¹ of said second peptide sequence are different amino acid
3 residues.

1 **44** (currently amended): The library according to claim **35**, wherein AA² of said
2 first peptide sequence and AA² of said second peptide sequence are identical amino acid
3 residues.

1 **45** (currently amended): The library according to claim **35**, wherein AA² of said
2 first peptide sequence and AA² of said second peptide sequence are different amino acid
3 residues.

1 **46** (currently amended): The library according to claim **35**, wherein AAⁱ of said
2 first peptide sequence and AAⁱ of said second peptide sequence are identical amino acid residues.

1 **47** (currently amended): The library according to claim **35**, wherein AAⁱ of said
2 first peptide sequence and AAⁱ of said second peptide sequence are different amino acid residues.

1 **48** (original): The library according to claim **42**, comprising at least six peptides
2 having different peptide sequences, wherein AA¹ is a different amino acid residue in each of said
3 different peptide sequences.

1 **49** (original): The library according to claim **48**, comprising at least twelve
2 peptides having different peptide sequences wherein AA¹ is a different amino acid residue in
3 each of said different peptide sequences.

1 **50** (original): The library according to claim **49**, comprising at least twenty
2 peptides having different peptide sequences wherein AA¹ is a different amino acid residue in
3 each of said different peptide sequences.

1 **51** (currently amended): The library according to claim **35**, wherein AA¹ is a
2 member selected from the group consisting of Lys, Arg, Leu and combinations thereof.

1 **52** (currently amended): The library according to claim **35**, wherein *J* is a
2 member selected from the numbers from 4 to 8.

1 **53** (currently amended): The library of peptides according to claim **35**, wherein
2 at least one of said first peptide and said second peptide is cleavable by a protease into a
3 fluorescent moiety and the peptide sequence.

1 **54** (currently amended): The library according to claim **35**, comprising at least
2 10 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **55** (original): The library according to claim **54**, comprising at least 100
2 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **56** (original): The library according to claim **55**, comprising at least 1,000
2 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **57** (original): The library according to claim **56**, comprising at least 10,000
2 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **58** (original): The library according to claim **57**, comprising at least 100,000
2 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **59** (original): The library according to claim **58** comprising at least 1,000,000
2 peptides, wherein each of the peptide sequences is a different peptide sequence.

1 **60** (currently amended): The library according to claim **35**, wherein said first
2 peptide is located at a first region of a substrate and said second peptide is located at a second
3 region of a substrate.

1 **61** (currently amended): A method of determining a peptide sequence specificity
2 profile of an enzymatically active protease, said method comprising:

- 3 (a) contacting said protease with a library of peptides according to claim **35** in
4 such a manner whereby the fluorogenic moiety is released from the
5 peptide sequence, thereby forming a fluorescent moiety;
- 6 (b) detecting said fluorescent moiety;
- 7 (c) determining the sequence of said peptide sequence, thereby determining said
8 peptide sequence specificity profile of said protease.

1 **62** (original): The method according to claim **61**, further comprising (d)
2 quantifying said fluorescent moiety, thereby quantifying said protease.

1 **63** (original): A database comprising at least one set of peptide sequence
2 specificity data for a protease determined using a library according to claim **35**.

1 **64** (original): The database according to claim **63**, wherein said database is an
2 electronic database.

1 **65** (original): The database according to claim **64**, wherein said database is
2 distributed on a wide area network.

1 **66** (original): A database comprising at least one set of peptide sequence
2 specificity data for a protease determined using a method according to claim **61**.

1 **67** (original): The database according to claim **63**, wherein said database is an
2 electronic database.

1 **68** (original): The database according to claim **64**, wherein said database is
2 distributed on a wide area network.

1 **69** (currently amended): The method according to claim **61**, wherein said
2 protease is a member selected from the group consisting of aspartic protease, cysteine protease,
3 and serine protease.

1 **70** (original): The method according to claim **61**, wherein said protease is a
2 protease of a microorganism.

1 **71** (original): The method according to claim **70**, wherein said microorganism is
2 a member selected from the group consisting of bacteria, fungi, yeast, viruses, and protozoa.

- 1 **72** (original): The method according to claim **61**, further comprising (c)
2 quantifying the fluorescent moiety, thereby quantifying said protease.

73-83 (cancelled)